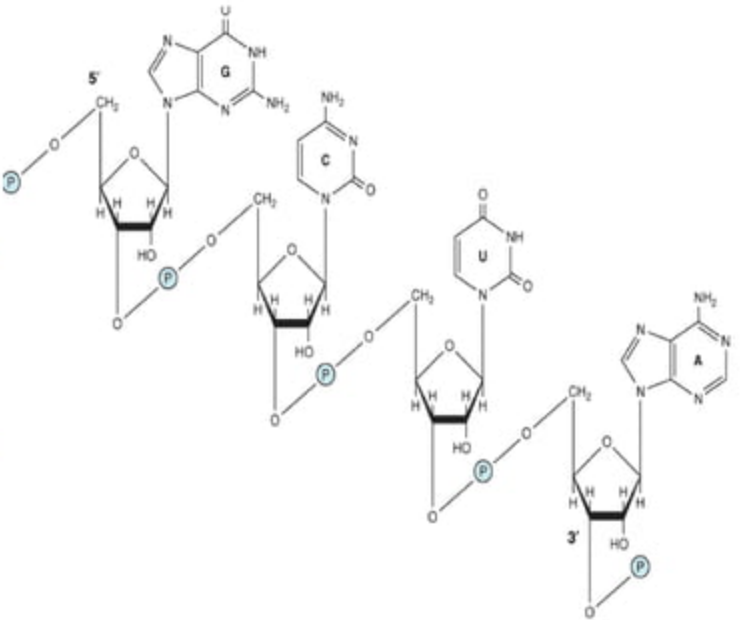
RNA STRUCTURE AND FUNCTIONS

Biochemistry for Medics

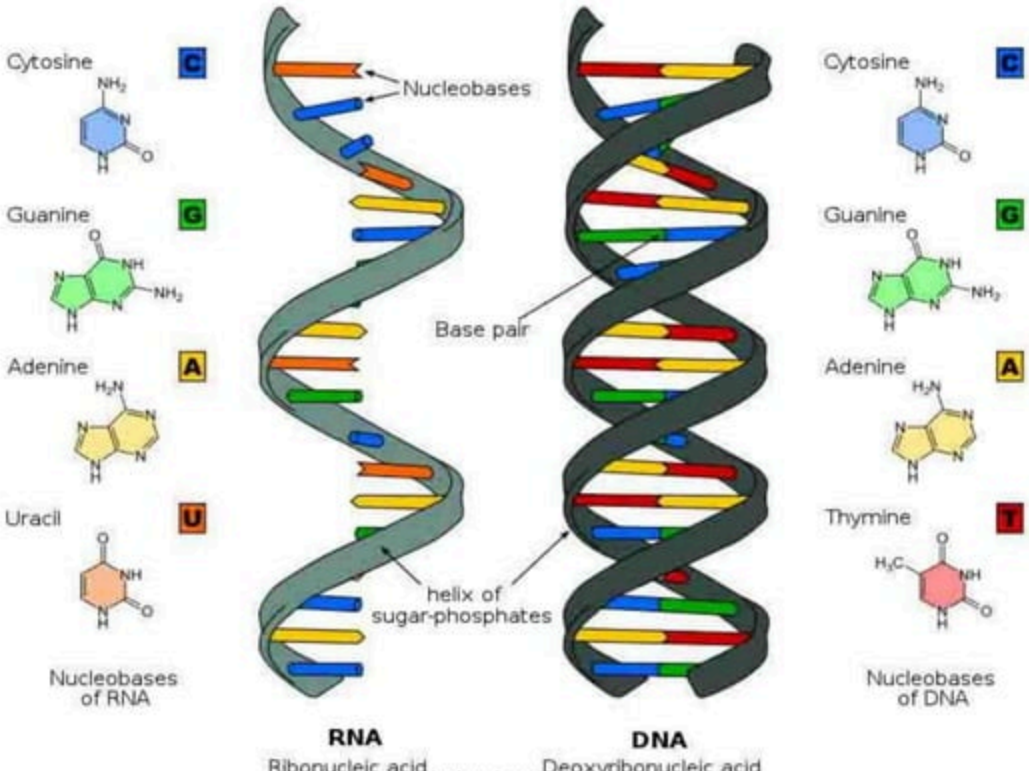
http://www.namrata.co/

RNA (Ribonucleic acid)

- RNA is a polymer of ribonucleotides linked together by 3’-5’ phosphodiester linkage



RNA V/S DNA


Cytosine
C
Guanine
G
Adenine
A
Uracil
U
Nucleobases of RNA
Nucleobases
Base pair
helix of sugar-phosphates
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid
Cytosine
C
Guanine
G
Adenine
A
Thymine
T
Nucleobases of DNA

Differences between RNA and DNA

S.No.	RNA	DNA
1)	Single stranded mainly except when self complementary sequences are there it forms a double stranded structure (Hair pin structure)	Double stranded (Except for certain viral DNA s which are single stranded)
2)	Ribose is the main sugar	The sugar moiety is deoxy ribose
3)	Pyrimidine components differ. Thymine is never found(Except tRNA)	Thymine is always there but uracil is never found
4)	Being single stranded structure- It does not follow Chargaff's rule	It does follow Chargaff's rule. The total purine content in a double stranded DNA is always equal to pyrimidine content.

Differences between RNA and DNA

S.No.	RNA	DNA
5)	RNA can be easily destroyed by alkalies to cyclic diesters of mono nucleotides.	DNA resists alkali action due to the absence of OH group at 2' position
6)	RNA is a relatively a labile molecule, undergoes easy and spontaneous degradation	DNA is a stable molecule. The spontaneous degradation is very 2 slow. The genetic information can be stored for years together without any change.
7)	Mainly cytoplasmic, but also present in nucleus (primary transcript and small nuclear RNA)	Mainly found in nucleus, extra nuclear DNA is found in mitochondria, and plasmids etc
8)	The base content varies from 100- 5000. The size is variable.	Millions of base pairs are there depending upon the organism

Differences between RNA and DNA

S.No.	RNA	DNA
9)	There are various types of RNA – mRNA, r RNA, t RNA, Sn RNA, Si RNA, mi RNA and hn RNA. These RNAs perform different and specific functions.	DNA is always of one type and performs the function of storage and transfer of genetic information.
10)	No variable physiological forms of RNA are found. The different types of RNA do not change their forms	There are variable forms of DNA (A to E and Z)
11)	RNA is synthesized from DNA, it can not form DNA(except by the action of reverse transcriptase). It can not duplicate (except in certain viruses where it is a genomic material)	DNA can form DNA by replication, it can also form RNA by transcription.
12)	Many copies of RNA are present per cell	Single copy of DNA is present per cell.

Types of RNA

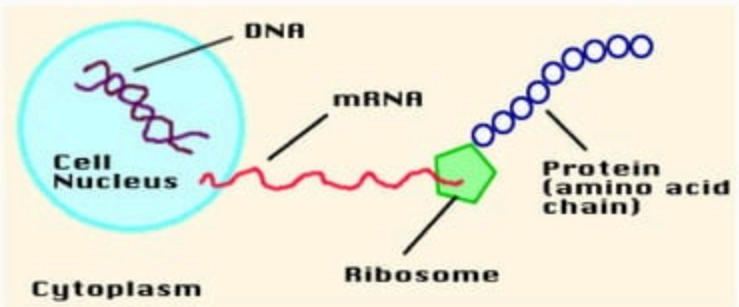
In all prokaryotic and eukaryotic organisms, three main classes of RNA molecules exist-

1) Messenger RNA(m RNA)
2) Transfer RNA (t RNA)
3) Ribosomal RNA (r RNA)

The other are –

- small nuclear RNA (SnRNA),
- micro RNA(mi RNA) and
- small interfering RNA(Si RNA) and
- heterogeneous nuclear RNA (hnRNA).

Messenger RNA (m-RNA)



- Comprises only 5% of the RNA in the cell
- Most heterogeneous in size and base sequence
- All members of the class function as messengers carrying the information in a gene to the protein synthesizing machinery

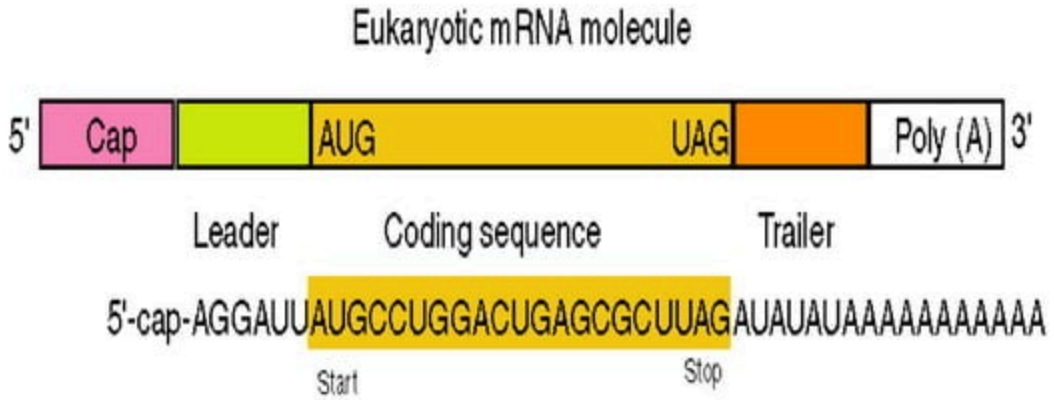
Structural Characteristics of m-RNA

- The 5’ terminal end is capped by 7-methyl guanosine triphosphate cap.
- The cap is involved in the recognition of mRNA by the translating machinery
- It stabilizes m RNA by protecting it from 5’ exonuclease

Structural Characteristics of m-RNA(contd.)

- The 3'end of most m-RNAs have a polymer of Adenylate residues(20-250)
- The tail prevents the attack by 3' exonucleases
- Histones and interferons do not contain poly A tails
- On both 5' and 3' end there are non coding sequences which are not translated (NCS)
- The intervening region between non coding sequences present between 5' and 3' end is called coding region. This region encodes for the synthesis of a protein.

Structural Characteristics of m-RNA



5’ cap and 3’ tail impart stability to m RNA by protecting from specific exo nucleases.

Structural Characteristics of m-RNA(Contd.)

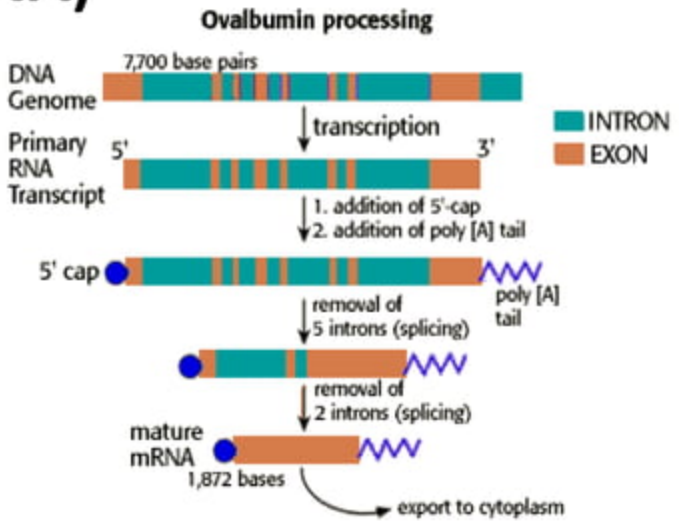
- The m- RNA molecules are formed with the help of DNA template during the process of transcription.
- The sequence of nucleotides in m RNA is complementary to the sequence of nucleotides on template DNA.
- The sequence carried on m -RNA is read in the form of codons.
- A codon is made up of 3 nucleotides
- The m-RNA is formed after processing of heterogeneous nuclear RNA

Heterogeneous nuclear RNA (hnRNA)

- In mammalian nuclei , hnRNA is the immediate product of gene transcription
- The nuclear product is heterogeneous in size (Variable) and is very large.
- Molecular weight may be more than $10^{7,}$ while the molecular weight of m RNA is less than $2x\ 10^{6}$
- 75 % of hnRNA is degraded in the nucleus, only 25% is processed to mature

m RNA

Heterogeneous nuclear RNA (hnRNA)



Mature m –RNA is formed from primary transcript by capping, tailing, splicing and base modification.

Transfer RNA (t- RNA)

- Transfer RNA are the smallest of three major species of RNA molecules
- They have 74-95 nucleotide residues
- They are synthesized by the nuclear processing of a precursor molecule
- They transfer the amino acids from cytoplasm to the protein synthesizing machinery, hence the name t RNA.
- They are easily soluble , hence called "Soluble RNA or s RNA
- They are also called Adapter molecules, since they act as adapters for the translation of the sequence of nucleotides of the m RNA in to specific amino acids
- There are at least 20 species of t RNA one corresponding to each of the 20 amino acids required for protein synthesis.

Structural characteristics of t- RNA

1) Primary structure- The nucleotide sequence of all the t RNA molecules allows extensive intrastand complimentarity that generates a secondary structure.

2) Secondary structure- Each single t- RNA shows extensive internal base pairing and acquires a clover leaf like structure. The structure is stabilized by hydrogen bonding between the bases and is a consistent feature.

Structural characteristics of t-RNA

Secondary structure (Clover leaf structure)

All t-RNA contain 5 main arms or loops which are as follows-

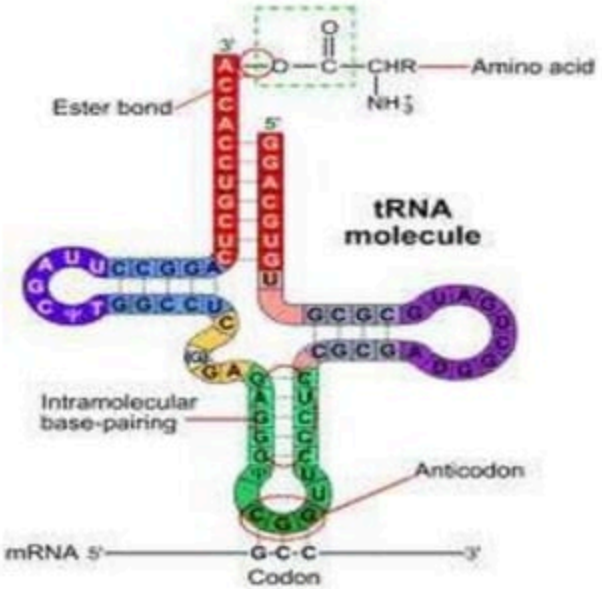
a) Acceptor arm
b) Anticodon arm
c) D HU arm
d) TΨ C arm
e) Extra arm

Secondary structure of t- RNA

a) Acceptor arm

- The acceptor arm is at 3' end
- It has 7 base pairs
- The end sequence is unpaired Cytosine, Cytosine-Adenine at the 3' end
- The 3' OH group terminal of Adenine binds with carboxyl group of amino acids
- The t RNA bound with amino acid is called Amino acyl t RNA
- CCA attachment is done post transcriptionally

Secondary structure of t- RNA



The carboxyl group of amino acid is attached to 3'OH group of Adenine nucleotide of the acceptor arm. The anticodon arm base pairs with the codon present on the m- RNA

Secondary structure of t-RNA(contd.)

b) Anticodon arm

- ❑ Lies at the opposite end of acceptor arm
- ❑5 base pairs long
- ❑Recognizes the triplet codon present in the m RNA
- ❑Base sequence of anticodon arm is complementary to the base sequence of m RNA codon.
- ❑ Due to complimentarity it can bind specifically with m RNA by hydrogen bonds.

Secondary structure of t-RNA(contd.)

c) DHU arm

- It has 3-4 base pairs
- Serves as the recognition site for the enzyme (amino acyl t RNA synthetase) that adds the amino acid to the acceptor arm.

d) TΨC arm

- This arm is opposite to DHU arm
- Since it contains pseudo uridine that is why it is so named
- It is involved in the binding of t RNA to the ribosomes

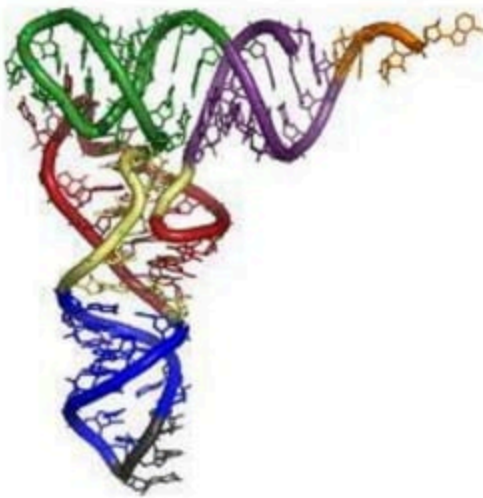
Secondary structure of t-RNA(contd.)

e) Extra arm or Variable arm

- About 75 % of t RNA molecules possess a short extra arm
- If about 3-5 base pairs are present the t-RNA is said to be belonging to class 1. Majority t -RNA belong to class 1.
- The t –RNA belonging to class 2 have long extra arm, 13-21 base pairs in length.

Tertiary structure of t- RNA

- The L shaped tertiary structure is formed by further folding of the clover leaf due to hydrogen bonds between T and D arms.
- The base paired double helical stems get arranged in to two double helical columns, continuous and perpendicular to one another.

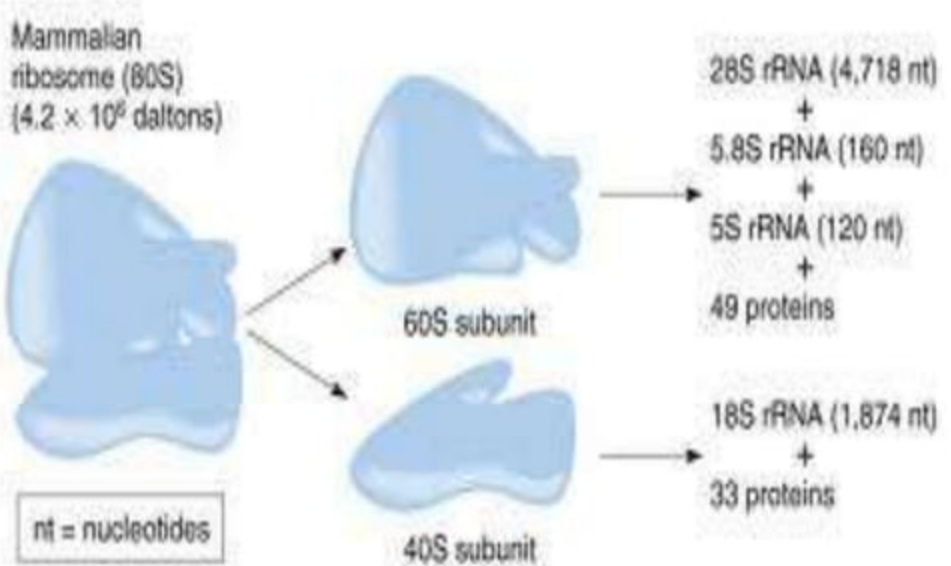


Ribosomal RNA (rRNA)

The mammalian ribosome contains two major nucleoprotein subunits—a larger one with a molecular weight of 2.8×10^6 (60S) and a smaller subunit with a molecular weight of 1.4×10^6 (40S).

- The 60S subunit contains a 5S ribosomal RNA (rRNA), a 5.8S rRNA, and a 28S rRNA; there are also probably more than 50 specific polypeptides.
- The 40S subunit is smaller and contains a single 18S rRNA and approximately 30 distinct polypeptide chains.
- All of the ribosomal RNA molecules except the 5S rRNA are processed from a single 45S precursor RNA molecule in the nucleolus .
- 5S rRNA is independently transcribed.

Ribosomal RNA (rRNA)



Ribosomal RNA (rRNA)

- The functions of the ribosomal RNA molecules in the ribosomal particle are not fully understood, but they are necessary for ribosomal assembly and seem to play key roles in the binding of mRNA to ribosomes and its translation
- Recent studies suggest that an rRNA component performs the peptidyl transferase activity and thus is an enzyme (a ribozyme).

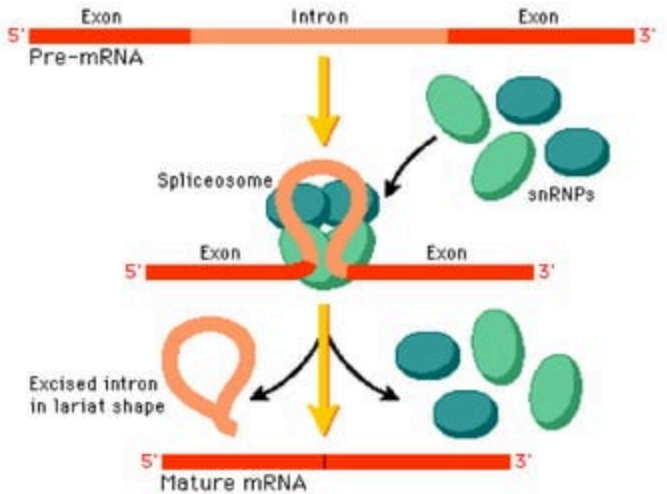
Small RNA

- Most of these molecules are complexed with proteins to form ribonucleoproteins and are distributed in the nucleus, in the cytoplasm, or in both.
- They range in size from 20 to 300 nucleotides and are present in 100,000–1,000,000 copies per cell.

Small Nuclear RNAs (snRNAs)

- snRNAs, a subset of the small RNAs, are significantly involved in mRNA processing and gene regulation
- Of the several snRNAs, U1, U2, U4, U5, and U6 are involved in intron removal and the processing of hnRNA into mRNA
- The U7 snRNA is involved in production of the correct 3' ends of histone mRNA—which lacks a poly(A) tail.

Small Nuclear RNAs (snRNAs).



Sn RNA s are involved in the process of splicing (intron removal) of primary transcript to form mature m RNA. The Sn RNA s form complexes with proteins to form Ribonucleoprotein particles called snRNPs

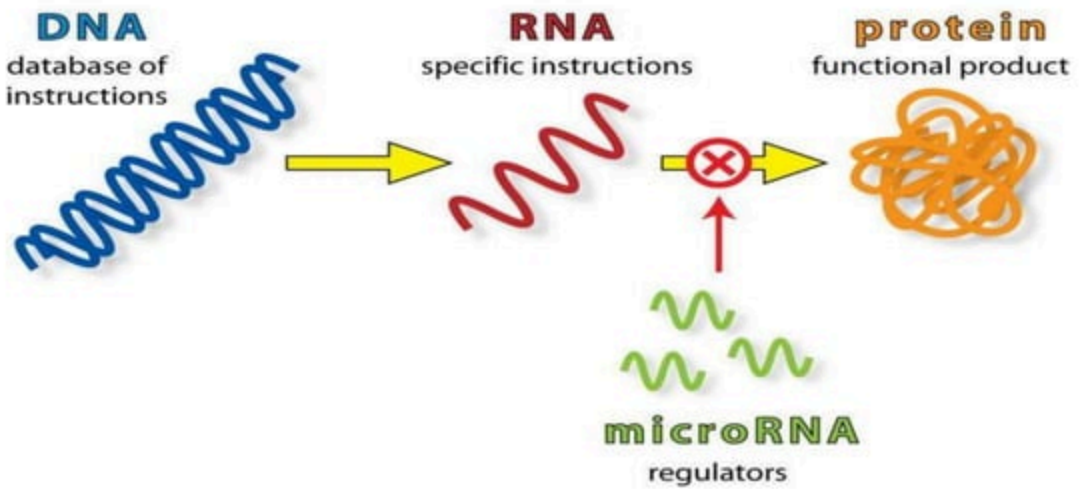
Micro RNAs, miRNAs, and Small Interfering RNAs, siRNAs

- These two classes of RNAs represent a subset of small RNAs; both play important roles in gene regulation.
- **miRNAs and siRNAs cause inhibition of gene expression** by decreasing specific protein production albeit apparently via distinct mechanisms

Micro RNAs (miRNAs)

- miRNAs are typically 21–25 nucleotides in length and are generated by nucleolytic processing of the products of distinct genes/transcription units
- The small processed mature **miRNAs typically hybridize, via the formation of imperfect RNA-RNA duplexes within the 3'-untranslated regions** of specific target mRNAs, **leading via unknown mechanisms to translation arrest.**

Micro RNAs (miRNAs)

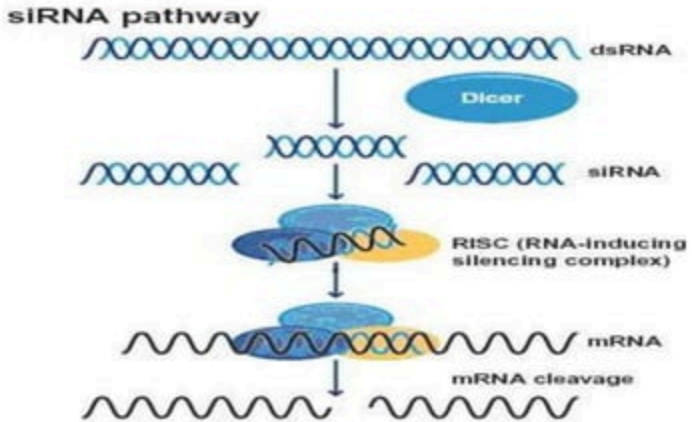


microRNAs, short non-coding RNAs present in all living organisms, have been shown to regulate the expression of at least half of all human genes. These single-stranded RNAs exert their regulatory action by binding messenger RNAs and preventing their translation into proteins.

Small Interfering RNAs (siRNAs)

- siRNAs are derived by the specific nucleolytic cleavage of larger, double-stranded RNAs to again form small 21–25 nucleotide-long products.
- These short **siRNAs usually form perfect RNA-RNA hybrids** with their distinct targets potentially anywhere within the length of the mRNA where the complementary sequence exists.
- Formation of such RNA-RNA duplexes between siRNA and mRNA results in reduced specific protein production because the **siRNA-mRNA complexes are degraded** by dedicated nucleolytic machinery;
- some or all of this mRNA degradation occurs in specific organelles termed P bodies.

Small Interfering RNAs (siRNAs)



Small interfering RNA (siRNA) are 20-25 nucleotide-long double-stranded RNA molecules that have a variety of roles in the cell. They are involved in the RNA interference (RNAi) pathway, where it interferes with the expression of a specific gene by hybridizing to its corresponding RNA sequence in the target mRNA. This then activates the degrading mRNA. Once the target mRNA is degraded, the mRNA cannot be translated into protein.

Significance of mi RNAs and si RNAs

- Both miRNAs and siRNAs represent exciting new **potential targets for therapeutic drug development in humans.**
- In addition, siRNAs are frequently used to decrease or "knock-down" specific protein levels in experimental procedures in the laboratory, an extremely useful and powerful alternative to gene-knockout technology.

Summary

- RNA exists in several different single-stranded structures, most of which are directly or indirectly involved in protein synthesis or its regulation.
- The linear array of nucleotides in RNA consists of A, G, C, and U, and the sugar moiety is ribose.
- The major forms of RNA include messenger RNA (mRNA), ribosomal RNA (rRNA), transfer RNA (tRNA), and small nuclear RNAs (snRNAs; miRNAs).
- Certain RNA molecules act as catalysts (ribozymes).
- miRNAs and siRNAs represent exciting new **potential targets for therapeutic drug development in humans.**